K2 cont.

said MAC117 gene or [increased] abnormal expression of said protein product of said MAC117 gene indicating a more malignant phenotype.

REMARKS

Claims 44, 46, 47 and 60-62 are pending in this application. Claims 44, 61 and 62 have been amended to more particularly define the invention. No new issues are raised because all of the amendments are of a clarifying nature only and are supported as set forth below. It is believed that no new matter has been added by these amendments. In light of these amendments and the following remarks, reconsideration and allowance of the pending claims to issue is respectfully requested.

Applicants note that claims 47, 61 and 62 are allowable over the prior art of record because of reasons of record.

Applicants wish to draw attention to the Attorney Docket number by which this file is now identified.

I. Rejection under 35 U.S.C. § 112, first paragraph

A. The specification is objected to and claims 44, 46, 47, 61 and 62 are rejected under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, allegedly does not provide support for the invention as now claimed. Specifically, the Office Action states that the amendments to the instant claims that are directed to "body sample" practice contain new matter because they are not also accompanied by detection of increased expression by antibodies as defined by originally filed claim 5. The Office Action notes that both the original claim 8, as filed and present claim 60 combine body sample detection practice with the performance of the detection via said antibodies and that the lack of this antibody detection limitation along with said "body sample" practice results in the rejected claims being broader in scope that the written basis for such body sample detection practice as filed. The Office Action goes on to state that this broader scope is new matter in that expression is inclusive of nucleic acid detection as well as detection practice such as that performed via binding of ligands to a receptor etc. and that this rejection is based on a lack of a written description of this broader "body sample" detection practice.

Applicants respectfully assert that no new matter has been added by the amendments to the pending claims. However, claims 44, 61 and 62 have been amended to clarify that

amplification and increased expression of the MAC117 gene can be detected in a tissue or tumor sample containing cells and that abnormal expression of the protein product of the MAC117 gene can be detected in a body sample, wherein the protein detection in a body sample is limited to reaction with antibodies. Thus, claims 44, 61 and 62 are now consistent with the language of claim 60, to which the Examiner has not objected on these grounds. For these reasons, applicants believe that this rejection is moot and respectfully request its withdrawal.

B. Claims 44, 46, 47 and 60-62 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is allegedly enabling only for claims limited to specific hybridization probes such as the insert in pMAC117 or the segment between Nco I and Acc I as cited on page 18, lines 12-26 and no antibody probes are enabled. The Office Action goes on to state that the reason for this rejection is the lack of instantly enabled epidermal growth factor (EGF) receptor protein. The Office Action explains that antibody probes must be prepared to distinguish MAC117 sequences and epitopes from very similar EGF receptor embodiments and that this can only be accomplished via the use of EGF receptor protein control samples to define those probes that are usable in the instant invention beyond those specifically instantly disclosed as to preparation. The Office Action goes on to state that this causes the EGF receptor protein to be essential subject matter to be required for broadly defined probes for negative control usage in selecting

MAC117 probes that do not also detect EGF receptor embodiments. The Office Action alleges that this rejection is maintained as given in the previous Office Action because although applicants argue that page 8 of the specification has been amended to include both nucleic acid sequence as well as protein sequence information, the amendment reveals that only a nucleic acid sequence has been added.

Applicants respectfully assert that anyone of ordinary skill in the art would readily be able to determine the amino acid sequence from the nucleotide sequence provided in the amendment to the specification, thus providing sufficient information to enable an artisan to practice the invention as claimed and that an additional amendment to incorporate the amino acid sequence is not necessary for such enablement. Thus, applicants believe this rejection to be moot and respectfully request its withdrawal.

II. Rejection under 35 U.S.C. § 112, second paragraph

A. Claims 44, 46, 47 and 60-62 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Office Action states that the rejected claims are vague and indefinite in that the metes and bounds of what applicants mean regarding the

practice of "a MAC117 gene" as cited in claim 44, line 3, or "the MAC117 gene" as cited in claim 60, lines 4 and 8, are not clearly defined. The Office Action inquires as to what set of characteristics limit what is meant by "a (or the) MAC117 gene." The Office Action points out that abnormal MAC117 genes are observable in some samples and poses the question as to how abnormal is still within the scope of what applicants mean regarding the gene. The Office Action cites one possible definition as that given in the specification on pages 4 and 9D, lines 2-5 and 10-12, respectively, where the scope of MAC117 gene practice is limited to genes containing the nucleotide sequence of Figure 1. The Office Action goes on to state it is unclear whether applicants mean the nucleotide sequence of Figure 1 to only be that sequence shown at the bottom cited as 424 bases in length or a gene containing at least the insert sequence of λMAC117 shown at the top of Figure 1, defined by a restriction map but not actually depicted as a detailed nucleotide sequence similar to that at the bottom of the figure. The Office Action notes that applicants present several arguments in support of clarifying the metes and bounds of the MAC117 gene but none of these arguments are deemed persuasive by the Examiner in overcoming this rejection and such clarification is still requested.

Claims 44, 61 and 62 have been amended to indicate that the MAC117 gene contains either a nucleotide sequence encoding the amino acids encoded by the 423 nucleotides set forth in Figure 1 or the restriction pattern set forth in Figure 5. As recognized by the Examiner, Figure 1 sets forth a 423 nucleotide sequence as an identifying characteristic of the MAC117 gene. Furthermore, Figure 5A shows the restriction map of cDNA of the MAC117 gene encompassing the entire coding region of the gene. Either of these characteristics define the metes and bounds of what is meant by the MAC117 gene as used in the claims. Since either of these characteristics can define a MAC117 gene of the claimed invention, the amendment is proper and is believed to overcome the rejection under 35 U.S.C. § 112, second paragraph. Applicants therefore respectfully request its withdrawal.

B. The Office Action states that claim 44 recites the intended method to be directed to "diagnosing or evaluating" in line 1 but only accomplished in recited steps what is deemed "diagnosing" in line 6 recited therein as "indicating the presence of cancer or a cancer with a more malignant phenotype." The Office Action acknowledges that evaluation might be construed to be correlated to the extent of amplification or increased expression of a MAC117 gene but that the evaluation criteria that correlate the extent of cancer seriousness to MAC117 amplification or increased expression are not evident from the claim but become possible interpretations after contemplating the claim wording at length. The

Office Action states that applicants' argument, that the phrase amended into claim 44 directed to a "cancer with a more malignant phenotype" corresponds to the evaluating of line 1 therein, is nonpersuasive because implied and unclear interpretations of claim wording fail to meet the requirements of 35 U.S.C.§ 112, second paragraph. The Office Action further states that because claim 44 lacks any statement that defines what is meant regarding "increased" expression, it is not clear from the claim what is meant regarding the "evaluating" practice and that a number of possible implied but not clearly set forth interpretations are possible for the practice of claim 44 etc. thus making the metes and bounds of its practice unclear as previously rejected.

Claim 44 has been amended, consistent with claim 60, such that "increased" has been changed to "abnormal" with regard to expression of the protein product. Further, claim 44 has been amended to clarify the diagnosis vs. more malignant phenotype determination. Specifically, claim 44 now states that the presence of amplification or increased expression of the MAC117 gene or abnormal expression of the protein product of the MAC117 gene indicates the diagnosis of cancer and the presence of amplification or increased expression of the MAC117 gene or abnormal expression of the protein product of the MAC117 gene indicates the presence of cancer with a more malignant phenotype. Support for this amendment is found in the specification on

page 23, lines 14-27. These amendments are believed to render moot the Examiner's rejections, and withdrawal of this basis of rejection is respectfully requested.

III. Rejection under 35 U.S.C. § 102 (a)

Claims 44, 46 and 60 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by either Semba et al. or Yamamoto et al. Specifically, the Office Action states that Semba et al. discloses the amplification of c-erbB-2 in human adenocarcinoma of the salivary gland, which reads on the diagnostic methods as instantly claimed for the carcinomas therein analyzed. The Office Action further states that Yamamoto et al. discloses c-erbB-2 amplification in cancer cells, suggesting that such amplification is sometimes involved in the neoplastic process and reading on the above rejected claims. The Office Action points out that these references were published less than one year prior to the parent application, serial number 06/836,414, thus making a 102(a) rejection appropriate due to priority given to the parent application for the subject matter of the above rejected claims. The Office Action notes that applicants argue that the instant invention was conceived and reduced to practice prior to the publication dates of the above listed references and submit an unsigned Declaration under 37 C.F.R. § 1.131 as evidence of this. The Office Action alleges that this is non-persuasive in overcoming the rejection because an unsigned Declaration is insufficient and because there is lacking a statement that the conception and reduction to practice of the instant invention occurred in the United States as required for such Declarations to be effective in overcoming the rejection as set forth.

Applicants respectfully point out that the above-mentioned Declaration was signed and forwarded to the U.S. Patent and Trademark Office on April 12, 1995, along with a Communication and the two other executed Declarations described in the April 4, 1995 Amendment filed with the Patent Office in connection with the instant patent application. Copies of these documents are included herewith. In addition, because the cited reference was submitted to a journal in the United States and was published in the United States, it is clear from the Declaration that the inventors' conception and reduction to practice occurred in the United States, and that a written statement by the inventors that the conception and reduction to practice of the instant invention occurred in the United States is not necessary, because the previously submitted Declaration is adequate for this purpose. Applicants therefore believe this rejection to be moot and respectfully request its withdrawal and allowance of the pending claims to issue.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A check in the amount of $1650.00 ($750.00 for the fee under 37 C.F.R. § 1.17(r) for filing a submission after final rejection under 37 C.F.R. § 1.129(a) and $900.00 for the three month extension of time after filing of the Notice of Appeal) is enclosed. This amount is believed

to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: BOX AF, Assistant Commissioner of Patents, Washington, D.C. 20231, on this 10 day of June, 1995.

David G. Perryman — 6-10-96 Date

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